Apheresis

**Objectives:**
- Explain the concept of cell centrifugation
- Explain the concept of extracorporeal volume
- Name 2 methods of venous access for apheresis

**What is Apheresis?**

**Elements:**
- Whole blood removal
- Separation by centrifugation
- Cells removed, replaced or reinfused.

**General Apheresis**

- **Elements:**
  - Whole blood removal
  - Separation by centrifugation
  - Cells removed, replaced or reinfused.

**Types of Apheresis**

- **Therapeutic**
  - Plasma Exchange
  - RBC Exchange
  - PLT Depletion
  - WBC Depletion
  - Photopheresis a.k.a ECP
  - LDL Apheresis

- **Collection**
  - Red Blood Cells
  - Plasma
  - Platelets
  - White Blood Cells

**Key Concept: Separation by Centrifugation**
Key Concept: Separation by Centrifugation

- **Key Concept:** Extracorporeal Volume (ECV)
  - ECV = amount of whole blood in the apheresis circuit
  - Average 250mL
  - Can be as much as 450mLs with some circuits
  - Regulations prohibit removing > 15% of total blood volume
  - Sometimes only 10% if safe for the patient
  - One size circuit, but may not fit all bodies
  - Blood prime option
  - ECV impacts patient oxygenation

Key Concept: Anticoagulation

- **ACD-A** (anticoagulant citrate dextrose, formula A)
  - Binds ionized calcium
  - Side-effect: ↓Ca, ↓K, ↓Mg
  - Short-acting / regional

**Heparin**

- Potentiates plasma antithrombin
- Long-acting
- Systemic anticoagulation

Key Concept: High-Flow Venous Access

- **Peripheral Venous Access**
  - 18g or bigger
  - AC veins best
  - Limited mobility
  - AV Fistula Needle
  - IV catheter
  - Usually for donors

- **Central Venous Access**
  - **Requirements**
    - Dual-lumen
    - High-flow
    - Short length
    - 10 - 14 Fr
    - Intra-jugular
  - **Tunneled:** Hickman-type
    - Patients
    - **Non-tunneled:** Mahurkar-type
    - Donors or collecting for storage

Fast, continuous blood flow
- Up to 150 ml/minute
- Uninterrupted blood flow for 2-6 hours
General Apheresis Side Effects

- Citrate Toxicity
- Vasovagal reaction
- Bleeding
- Blood Loss
- Transfusion needs
- Allergic Reactions (ETO)
- Fatigue

Citrate Toxicity

Feels like:
- Lips tingling, body vibration, cramps, chest pain

Looks like:
- Low ionized calcium, pallor, tetany

Resolve:
- Pause the procedure – resume using slower flow rate
- Oral replacement – TUMS, orange juice, calcium-rich food
- IV replacement – calcium gluconate
- Required: ionized calcium point-of-care testing

Pediatric Issues

Small body, big circuit
- Prime the apheresis circuit with packed RBCs

Side-effects are subtle, fast and strong

IV access:
- usually central
- Peripheral access is possible in larger children (40-50 kg) when patient is highly motivated

HPC-A Collection Specifics

Hematopoietic Progenitor Cells - Apheresis

Type of White Blood Cell Collections (leukapheresis)

**Hematopoietic Progenitor Cell (HPC)**
- a.k.a Peripheral Blood Stem Cell (PBSC)

**Bone Marrow – Red Blood Cell Reduction**
- Reduce marrow volume and RBC content
- Donor / Recipient incompatible ABO

**Lymphocytes (DLI = donor lymphocyte infusion)**
- From original donor, infused to recipient to induce mild GvHD

**Mononuclear Cells**
- Usually targeting lymphocytes
- T-cells, dendritic cells
- Immunotherapy

Autologous Preparation

- Consent
- Venous Assessment
- H&P
- Infectious Disease Testing
- ABO typing
- Storage contract
Allogeneic Preparation

- Consent
- Venous Assessment
- H&P
- ABO typing / recipient compatibility
- Females - pregnancy testing pre-GCSF
- Donor History Questionnaire
- Infectious Disease Testing
- Donor Eligibility Declaration
  - Eligible / Ineligible, Suitable / Unsuitable
  - Justification for Urgent Medical Need

HPC-A Mobilization

Stem cells move from marrow to blood circulation
- Chemotherapy
- Chemotherapy + G-CSF
- Plerixafor (Mozobil)
  - At SCCA – 4th day of G-CSF injection
  - Repeat up to 4 consecutive days
  - Administered SQ ~ 11 hours prior to apheresis

Procedure Qualification Parameters

**Autologous HPC-A Collections**
- HCT ≥ 28%
- PLT ≥ 20K – 50K
  - Depends on volume processed

**Allogeneic HPC-A Collections**
- HCT ≥ 35%
- PLT ≥ 110,000/μL

* Order to proceed required if lab parameters not met *

Patient / Donor Education

Pre-procedure instructions
- Eat pre-procedure: calcium-rich food
- Be warm
- Increase fluid intake
- Hold meds
  - Anticoagulants
  - Antihypertensives
- Bring entertainment!

HPC-A Collection Timing

**Protocol driven**

**Autologous collection trigger**
- Peripheral CD34 level (PBL) > 10 uL
- Day after WBC > 1,000 uL
- 4th day of G-CSF mobilization

**Allogeneic collection trigger**
- 4th day of G-CSF mobilization

HPC-A Cell Collection Goals

**Protocol and diagnosis driven**

**Allogeneic targets dependent on recipient’s protocol:**
- non-myeloablative vs. myeloablative transplant
- specific cell quantity
  - typically 5 x 10^6 CD34^+ / kg recipient weight
  - Some protocols require 2 collections regardless of cell quantity achieved on Day 1

**Autologous targets**
- Myeloma: 10 x 10^6 CD34^+ / kg
- NHL: 5 x 10^6 CD34^+ / kg
Allogeneic HPC-A Collection Process

Day 1:
- Donor PBSC collection
- Overnight cell storage for Day 0 infusion

Day 0:
- 2nd collection if Day 1 goal not met or if required by protocol
- Cells from both days of collection infused to recipient

HPC Collection: Procedure Length

Flow rate and blood volume processed impact collection time
- Standard Volume = 12 L
  - 2-3 hours
- Large Volume = 6 x total blood volume
  - 4-5 hours

Regulatory Oversight

In addition to patient care regulation (TJC, DOH), we are manufacturing and transplanting human cells and tissues, and are regulated by:

FDA – Food and Drug Administration.
  - Federal laws that must be followed

FACT – Foundation for the Accreditation of Cellular Therapy
  - Voluntary quality assurance organization granting accreditation

CAP – College of American Pathologists
  - Quality control for laboratory aspects of apheresis

Regulation vs. Accreditation

Regulation
- Law
- 100% Compliance Expectation

Accreditation
- Recognition
- Certification
- Improves performance and safety

Noncompliance can result in non-payment by insurance, program closure, fines, jail

ECP – Indications

- FDA indicated for use in the palliative treatment of skin manifestations of Cutaneous T-Cell Lymphoma (CTCL) that are unresponsive to other forms of treatment.
- Off-label use:
  - GvHD
  - Solid-organ transplant rejection: lung, heart, liver
  - Scleroderma
  - Crohn’s Disease
Mechanism of Action – proposed!

- **EX VIVO:**
  - Uvadex® injected into collected WBC product
  - UVA light activates Uvadex®
  - Uvadex® causes DNA cross-linking in nucleated cells → apoptosis

Apoptosis
- Programmed cell death
- Immune pathway regulating cell cycle

Mechanism of Action - proposed

- **IN VIVO:**
  - Infused apoptotic cell population induces APC cell response
  - Triggers anti-inflammatory response pathway
    - Increased production of Regulatory T-Cells
    - Decreased production of Effector T-Cells
  - Results in tolerance

Antigen Presenting Cell (APC)

Treatment Regimens

- Usually 2 days per week
- Labeling is for consecutive days
- Labeling is for CTCL
  - Monthly x 6 months
- Off-label at SCCA
  - Acute GvHD
    - Weekly x 8 weeks
    - 3 days weekly x 12 weeks (upcoming Acute Peds GvHD Trial)
  - Chronic GvHD
    - Weekly x 4 weeks → bi-weekly x 3-6 mos. → monthly
  - Solid-organ Transplant Rejection
    - Weekly x 1 mo. → bi-weekly x 1 mo. → monthly for 4 mos.

ECP - Process

- A leukapheresis procedure:
  - WBCs isolated from whole blood
  - Uvadex® mixed with WBCs
  - UVA light activates Uvadex®
  - WBCs reinfused to the patient

Photoactivation Module

- Buffy coat is exposed to UVA lights as it circulates through the module
- Buffy coat recirculates multiple times to receive adequate UVA exposure
  - Average photoactivation time = 20”

Venous Access

- Device must allow 50 mL / minute flow rates
- Needs to be reliably patent
Side Effects

- **Common**
  - Fatigue
  - Photosensitivity

- **Less Common**
  - Citrate Toxicity
  - Hypotension
  - Fluid overload
  - Bleeding
  - Blood Loss
  - Anemia
  - Infection

Apheresis: Services and Volumes

In 2016, APH performed:

- 583 HPC-A collections
- 251 Research collections
- 7 DLI collections
- 11 HPC-M RBC reductions
- 1283 Extracorporeal Photopheresis (ECP) procedures
- 31 Plasma Exchange procedures

Thank you!